

disruption prevents expression of functional  $\alpha$ -1,3 galactosyltransferase.

47. The DNA construct of claim 46, wherein said disruption is within exon 4, exon 7, exon 8, or exon 9 of the porcine  $\alpha$ -1,3 galactosyltransferase gene.

48. The DNA construct of claim 46, wherein said exogenous sequence is a selectable marker.

49. The DNA construct of claim 48, wherein said selectable marker is selected from the group consisting of the neo<sup>R</sup> gene and the hyg<sup>R</sup> gene.

50. The DNA construct of claim 46, wherein said exogenous sequence is flanked at its 5' and 3' ends by FRT DNA elements, and wherein stop codons have been inserted 3' to the selectable marker for each of the three reading frames for the porcine  $\alpha$ -1,3 galactosyltransferase gene.

51. A method for generating a porcine cell comprising at least one inactivated  $\alpha$ -1,3 galactosyltransferase gene, the method comprising:

- (a) providing a plurality of porcine cells;
- (b) introducing into said cells a DNA construct comprising a disrupted porcine  $\alpha$ -1,3 galactosyltransferase gene, wherein the disruption is by the insertion of an exogenous sequence into said gene such that the disruption prevents expression of functional  $\alpha$ -1,3 galactosyltransferase;
- (c) incubating said cells such that homologous recombination occurs between the chromosomal sequence encoding  $\alpha$ -1,3 galactosyltransferase and the introduced DNA construct comprising the disrupted  $\alpha$ -1,3 galactosyltransferase gene; and

(d) identifying a porcine cell comprising at least one inactivated  $\alpha$ -1,3 galactosyltransferase gene.

52. The method of claim 51, wherein said cell is a porcine ES cell.

53. The method of claim 51, wherein said cell is a porcine PGC.

54. The method of claim 51, wherein said porcine cell is a porcine egg.

55. A method for generating a pig homozygous for an inactivated  $\alpha$ -1,3 galactosyltransferase gene comprising:

(a) providing a porcine cell comprising at least one inactivated  $\alpha$ -1,3 galactosyltransferase gene;

(b) manipulating said cell such that mitotic descendants of said cell constitute all or part of a developing embryo;

(c) permitting said embryo to develop into a neonatal pig;

(d) permitting said neonate to reach sexual maturity;

(e) mating said sexually mature pig to obtain a pig homozygous for said inactivated  $\alpha$ -1,3 galactosyltransferase gene, wherein said homozygous genes result in a pig that lacks the GAL epitope as determined by the failure of said pig's somatic cells to bind anti-GAL antibodies and IB4 lectin, and by the increased resistance of said cells, relative to cells from a wild type pig, to be lysed by human serum.

56. The method of claim 55, wherein said cell is a porcine ES cell and said manipulating comprises injecting said ES cell into a blastocyst cavity of a porcine blastocyst and

implanting said injected blastocyst into a porcine recipient female.

57. The method of claim 55, wherein said cell is a porcine ES cell and said manipulating comprises injecting said ES cell into a porcine morula.

58. The method of claim 55, wherein said cell is a porcine ES cell and said manipulating comprises co-culture of said ES cell with a zona pellucida-disrupted porcine morula.

59. The method of claim 55, wherein said manipulating comprises fusing said porcine cell with an enucleated porcine oocyte.

60. The method of claim 55, wherein said cell is a porcine egg, and said manipulating comprises implanting said egg into a porcine recipient female.

61. A pig homozygous for an inactivated  $\alpha$ -1,3 galactosyltransferase gene produced by the method of claim 55.

62. A pig homozygous for an inactivated  $\alpha$ -1,3 galactosyltransferase gene, wherein said inactivation is by the insertion of an exogenous sequence into said gene and wherein said homozygous inactivation results in a pig that lacks the GAL epitope as determined by the failure of said pig's somatic cells to bind anti-GAL antibodies and IB4 lectin, and by the increased resistance of said cells, relative to cells from a wild type pig, to be lysed by human serum.

63. Cells isolated from the pig of claim 61, wherein said cells lack the GAL epitope as determined by the failure of said cells to bind anti-GAL antibodies and IB4 lectin, and by the